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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,155	10/12/2001	Joachim Herz	UTSD:0862	3854

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,155	HERZ ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-20* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicants' response to the Office Action mailed 12/7/04 is acknowledged. In the amendment filed therein claims 1 and 11 were modified. Applicant's supplemental response filed 3/9/05 is acknowledged. Currently claims 1-20 are pending and under consideration.

2. Rejections and/or objections of record not reiterated below have been withdrawn.

OBJECTIONS WITHDRAWN

Information Disclosure Statement

3. Examiner pointed out the unrelated art of record in the information disclosure statement (IDS) filed 02 April 2004 (Paper #5, item 7). Applicants have confirmed that they have not filed the IDS and request that the document is removed from the instant file. Examiner has provided an attached/updated PTO-1449, indicating that the IDS is not apart of the instant application. Accordingly the objection is withdrawn.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1-9 and 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Willnow et al. (The Journal of Biological Chemistry, Vol.269, No.22,15827-15832, 1994).

Willnow et al. teach methods involving LRP-mini receptors . See abstract. The LRP-mini receptor comprises 11 complement-type repeats (LDL receptor ligand – polypeptide) and one EGF precursor homologous domain (region IV) is fused to the carboxyl-terminal segment of LRP (six EGF repeats, transmembrane segment, and the cytoplasmic tail). See page 5828, 2nd column, 1ts paragraph, and figure 1. Region IV contains a proteolytic site, which allows for protease digestion into a 80kDa amino-terminal and a 85kDa carboxyl-terminal fragment (C-terminal tail).

The LRP regions were prepared via SDS gel electrophoresis and transferred to nitrocellulose (solid-phase affinity adsorption). Polyclonal anti-LRP antibodies directed against the cytoplasmic tail of LRP and ^{125}I goat anti-rabbit IgG (affinity tag) were utilized in Western blotting procedures to detect the mini receptors membrane extracts from the cell lines. Bottom of page 15828 to 15829 and figure 2.

Response to Arguments

Applicant contends that Willnow et al. describes truncated LRPs comprising subsets of the native N-terminal domains. Therefore the proteolytic process does not occur at intramembraneous or cytoplasmic sites to liberate a cytoplasmic tail. This argument was carefully considered but not found persuasive because Willnow et al. disclose LRPs subsets that include the cytoplasmic tail as well as the detection of the cytoplasmic tail. For example on page 15828, 2nd column, middle section and figure 1 - regions II and IV are fused to the membrane (carboxyl-terminal segment) and the cytoplasmic tail (cytoplasmic segments of LRP).

Proteolytic processing resulting in a separation of the LRP within the domain to produce a N-terminal and C-terminal product is seen on page 15829 1st column. In one embodiment, the cytoplasmic tail of LRP is detected with polyclonal anti-LRP antibodies by Western blotting. See page 15828 2nd column 2nd paragraph.

On page 15829, 1st column, 1st paragraph – Region IV is taught to be cleaved by intracellular proteases that cleave LRP at a tetrabasic site in the eighth EGF precursor domain and these proteases can process LRP into a 80kDa amino terminal and a 85kDa carboxyl-terminal fragment (lanes 2 and 4 of figure 2A). Accordingly, Willnow et al. teach proteolysis procedures that produce a N-terminal and C-terminal of a LDL receptor domain fused to a c-terminal tails and well as c-terminal tail detection.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a cytoplasmic tail released at intramembraneous or cytoplasmic sites) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims merely require a protease that cleaves the domain.

In the supplemental response faxed 3/9/05, Applicants contend that Willnow et al. describe LRP cleavage at an N-terminal and no theoretical concept or experimental data is disclosed to suggest the release of the C-terminal tail from the membrane. This argument has been carefully considered but not found persuasive because Willnow et al. teach C-terminal tail liberation and detection. See page 15828 2nd column through page 15829 1st column.

Further, a reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1966). *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willnow et al. (The Journal of Biological Chemistry, Vol.269, No.22,15827-15832, 1994) in view of Herz (Neuron, Vol29, pages 571-581).

Please see Willnow et al. as set forth above.

Willnow et al. differs from the instant invention in not teaching all the possible LDL receptor (namely LRP, LRP1b, megalin, LDLR, VLDLR,ApoER2, MEGF7, LRP5, LRP6, and LR11).

However, Herz discloses the core members of the LDL receptor gene. See abstract and figure 1. Herz further teaches each LDL possible role and involvement in cellular events. See Table 1. The core members of the LDL receptor gene family include the LDL receptor, LRP, megalin, VLDL, ApoER2, LrP1b, and MEGF7. See page 571, 1st column, 2nd paragraph. Herz et al. disclose that these seven core members of the LDL receptor gene family are "structurally closely related cell surface receptor".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use various known LDL receptor equivalents having similar structures and found native to the membrane as taught by Herz in the method of Willnow et al. because Herz taught that the LDL receptor gene family consists of seven structurally related cell surface receptors (LDL receptor, LRP, megalin, VLDL, ApoER2, LrP1b, and MEGF7). See abstract. Therefore the analysis of any of the known equivalent receptors taught by Herz in the method of Willnow et al. would have been obvious because the receptors would perform the same function in the same manner as the receptors found in Willnow et al. In other words the behavior of one compound predicts the behavior of equivalents absent evidence to the contrary. Further, applicant has not set forth reasons for the utility of any particular receptor.

Accordingly, obviousness is based on the similarity of structure, function, and similar properties. In re Payne, 606 F.2d 303, 203, USPQ 245, 254-55 (CCPA 1979).

Response to Arguments

Applicants argue that Willnow et al. do not teach protease liberation of the c-terminal tail of LDR, therefore the combination of Willnow et al. and Herz et al. cannot make the invention obvious. This argument has been carefully considered but is not found persuasive. The arguments against Willnow et al. have been addressed a priori and were not found persuasive, therefore the rejection of Willnow et al. in view of Herz et al. is maintained.

Allowable Subject Matter

6. Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Remarks

7. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure: Tan et al. (Biochimica et Biophysica Acta, 7/1/98, Vol1407, No1, pages 69-78) Abstract Only - disclose constructs including an LDL receptor.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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05/16/05